

Listing of Claims:

1-7. (Cancelled)

8. (Original) A method of identifying an agonist or an antagonist of a co-regulator dependent target molecule comprising providing a set of molecules that shift the thermal unfolding curve of the target molecule and screening one or more of said molecules of said set for their ability to further shift the thermal unfolding curve of the target molecule in the presence of one or more coregulators; wherein a further shift in the thermal unfolding curve of the target molecule in the presence of a molecule of said set and a co-regulator of said one or more co-regulators indicates whether the molecule is an agonist or an antagonist of the target molecule when in the presence of said co-regulator.

9. (Original) The method of claim 8, wherein providing the set of molecules that shift the thermal unfolding curve of the target molecule comprises screening one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule.

10. (Original) The method of claim 9, wherein the screening of said one or molecules of said set of molecules for their ability to further shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule and one or more molecules of said set with one or more of said co-regulators in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of (i) any of said molecules of said set and/or (ii) said co-regulators; and

(f) determining whether any of said molecules of said set further shift the thermal unfolding curve of said target molecule.

11. (Original) The method of claim 10, wherein the screening of said one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of any of said multiplicity of different molecules; and determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said target molecule.

12. (Original) The method of claim 8, wherein said one or more co-regulators includes a co-activator and/or a co-repressor.

13. (Original) The method of claim 12, wherein one or more molecules of the set further shift the thermal unfolding curve of the target molecule in the presence of a co-activator, thereby identifying an agonist of the target molecule when in the presence of the co-activator.

14. (Original) The method of claim 12, wherein the one or more molecules of the set further shift the thermal unfolding curve of the target molecule in the presence of a co-repressor, thereby identifying an antagonist of the target molecule when in the presence of the co-repressor.

15-18. (Cancelled)

19. (Original) A method of identifying an antagonist of a co-regulator-dependent target molecule comprising providing a set of molecules that shift the thermal unfolding curve of the target molecule and screening one or more of said molecules of said set for their ability to further shift the thermal unfolding curve of the target molecule in the presence of one or more co-activators; wherein no further shift in the thermal unfolding curve in the presence of a molecule of said set and a co-activator of said one or more co-activators indicates that the molecule of said set is an antagonist of the target molecule when in the presence of said co-activator.

20. (Original) The method of claim 19, wherein providing the set of molecules that shift the thermal unfolding curve of the target molecule comprises screening one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule.

21. (Original) The method of claim 20, wherein the screening of said one or more molecules of said set of molecules for their ability to further shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule and one or more molecules of said set with one or more of said co-activators in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of (i) any of said molecules of said set and/or (ii) said co-activators; and

(f) determining whether any of said molecules of the set further shift the thermal unfolding curve of said target molecule.

22. (Original) The method of claim 21, wherein the screening of said one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of any of said multiplicity of different molecules; and

(f) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said target molecule.

23-26. (Cancelled)

27. (Original) A method of identifying an agonist of a co-regulator-dependent target molecule comprising providing a set of molecules that shift the thermal unfolding curve of the target molecule and screening one or more of said molecules of said set for their ability to further shift the

thermal unfolding curve of the target molecule in the presence of one or more co-repressors; wherein no further shift in the thermal unfolding curve in the presence of a molecule of said set and a co-repressor of said one or more co-repressors indicates that the molecule of said set is an agonist of the target molecule when in the presence of said co-repressor.

28. (Original) The method of claim 27, wherein providing the set of molecules that shift the thermal unfolding curve of the target molecule comprises screening one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule.

29. (Original) The method of claim 28, wherein the screening of said one or molecules of said set of molecules for their ability to further shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule and one or more molecules of said set with one or more of said co-repressors in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of (i) any of said molecules of said set and/or (ii) said co-repressors; and

(f) determining whether any of said molecules of the set further shift the thermal unfolding curve of said target molecule.

30. (Original) The method of claim 29, wherein the screening of said one or more of a multiplicity of different molecules for their ability to shift the thermal unfolding curve of the target molecule comprises:

(a) contacting said target molecule with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(b) heating said multiplicity of containers;

(c) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(d) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers;

(e) comparing each of said thermal unfolding curves in step (d) to (1) each of the other thermal unfolding curves and/or to (2) the thermal unfolding curve for said target molecule in the absence of any of said multiplicity of different molecules; and

(f) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said target molecule.

31-34. (Cancelled)

35. (Currently Amended) The method of claim 8 ~~any one of claims 1-34~~, wherein the target molecule is a nuclear receptor.

36. (Currently Amended) The method of claim 8 ~~any one of claims 1-34~~, wherein the target molecule is a G-protein coupled receptor.

37. (Currently Amended) The method of claim 8 ~~any one of claims 1-30~~, wherein the target molecule is ER- α .

38. (Currently Amended) The method of claim 8 ~~any one of claims 1-30~~, wherein the target molecule is ER- β .

39. (Currently Amended) The method of claim 8 ~~any one of claims 1-30~~, wherein the target molecule is a tyrosine kinase.

40. (Currently Amended) The method of claim 8 ~~any one of claims 1-30~~, wherein the target molecule is a NF- κ B.